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Kathy Meuse
Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Richard F Selden et al.	Art Unit:	1636
Serial No.:	09/328,130	Examiner:	K. Katcheves
Filed:	June 8, 1999	CustomerNo.:	35093
Title:	In Vivo Production and Delivery of Erythropoietin or Insulinotropin for Gene Therapy		

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
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REPLY TO FINAL OFFICE ACTION

In reply to the final Office Action that was mailed in connection with the above-captioned case on February 11, 2003, applicants submit the following Remarks.

The only outstanding rejection in this case is an obviousness-type double patenting rejection over U.S. Patent No. 6,303,379 B1 (the "'379 patent"). In this rejection, the Examiner notes that the claims of the '379 patent are drawn to primary or secondary cells containing nucleic acid molecules encoding a therapeutic product, as well as methods of producing such cells, and that the present claims differ from those of the '379 patent only

in specifying that the therapeutic product is erythropoietin. The Examiner further states that the claims of the present application would have been obvious over the '379 claims, because those of ordinary skill in the art were aware that erythropoietin is a therapeutic product. This rejection should be withdrawn for the following reasons.

The fact that a protein is known to be therapeutic does not necessarily mean that it would be obvious to administer the protein using an *in vivo*, cell-based approach, such as that in which the cells of the present invention can be used. This approach to therapy simply is not appropriate for the administration of certain proteins. For example, it is imperative that certain therapeutic proteins be administered on a very short-term basis only. Continued production of such proteins in a patient after the condition intended to be treated has been alleviated, as could occur using *in vivo*, cell-based therapy methods, could be dangerous. For example, albumin is frequently administered on a short-term basis to accident victims who have experienced blood loss, in order to increase their serum protein levels. Administration of albumin beyond the period of the initial trauma, however, can lead to serious problems, such as impairment of heart function. Thus, albumin administration is not amenable to *in vivo*, cell-based therapy of trauma.

Prior to the present invention, it was thought that, as was the case for albumin and many other proteins, erythropoietin was to be administered by physicians only in a tightly controlled manner. It was thought that prolonged administration of erythropoietin, which results in increased hematocrit levels, would increase a patient's risk of heart attack and

stroke. Thus, clinicians were very cautious about the amounts of erythropoietin that they administered, and certainly would not have been motivated to administer erythropoietin using *in vivo*, cell-based therapy methods. Consistent with this prejudice, prior to the present invention, administration of erythropoietin to patients using *in vivo*, cell-based therapy methods had never been suggested, let alone attempted. Nothing in the record or in any document of which applicants are aware suggests that those persons and companies with an enormous academic or financial stake in erythropoietin held any notion that *in vivo*, cell-based delivery was a viable strategy for erythropoietin therapy. Indeed, all of the evidence demonstrates the opposite: a universal commitment to the injected erythropoietin approach, to the exclusion of other approaches. For example, Amgen Corporation possessed the erythropoietin gene since as early as 1983, published on the gene, and filed a number of patent applications relating to the erythropoietin gene. Yet in not a single one of these documents did Amgen, with its enormous incentive to optimize erythropoietin therapy, make the slightest mention of even the possibility of erythropoietin *in vivo*, cell-based therapy prior to applicants' disclosure. The possibility of such therapy simply was not mentioned in any scientific literature. It necessarily follows that the presently claimed primary and secondary cells stably transfected with the erythropoietin gene, which are to be used *in vivo* therapy methods, would not have been obvious at the time of applicants' invention. Applicants thus respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: February 11, 2004 Susan M. Michaud

Susan M. Michaud, Ph.D.
Reg. No. 42,885

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045